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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/511,776	02/24/2000	Roger K Craig	4256/86197	5653

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EXAMINER
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GABEL, GAILENE

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 12/16/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Applicant No.</b>	<b>Applicant(s)</b>	
	09/511,776	CRAIG ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 23 September 2002.
- 2a) This action is FINAL.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1,2,4-8 and 10-22 is/are pending in the application.
- 4a) Of the above claim(s) 15-18 is/are withdrawn from consideration.
- 5) Claim(s) 1,2,4-8 and 10-14 is/are allowed.
- 6) Claim(s) 19-22 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) 1,2,4-8 and 10-22 are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                               | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)           | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ .                                   |

**DETAILED ACTION**

***Continued Prosecution Application***

1. The request filed on 9/23/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/511,776 is acceptable and a CPA has been established. An action on the CPA follows.

***Amendment Entry***

2. Applicant's amendment and response filed 5/30/02 in Paper No. 13 is acknowledged and has been entered. Claims 1-2, 5, 13, 19-20, and 22 have been amended. Currently, claims 1-2, 4-8, and 10-22 are pending. Claims 15-18 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Claims 1-2, 4-8, 10-14, and 19-22 are under examination.

**Rejections Withdrawn**

**Claim Rejections - 35 USC § 102**

3. In light of Applicant's amendment and arguments, the rejection of claims 1, 4-8, and 12-13 under 35 U.S.C. 102(e) as being anticipated by Prusiner et al. (US 5,891,641) is hereby, withdrawn.

4. In light of Applicant's amendment and arguments, the rejection of claims 1, 4-8, and 12-13 under 35 U.S.C. 102(e) as being anticipated by Martinez et al. (WO 98/41872) is hereby, withdrawn.

Art Unit: 1641

5. In light of Applicant's amendment and arguments, the rejection of claims 1, 7-8, and 10-11 under 35 U.S.C. 102(e) as being anticipated by Tsien et al. (US 5,998,204) is hereby, withdrawn.

6. In light of Applicant's amendment and arguments, the rejection of claims 19-22 under 35 U.S.C. 103(a) as being unpatentable over Martinez et al. (WO 98/41872) or Tsien et al. (US 5,998,204) in view of Foster et al. (US 4,444,879) is hereby, withdrawn.

7. In light of Applicant's amendment and arguments, the rejection of claims 2 and 14 under 35 U.S.C. 103(a) as being unpatentable over 1) Prusiner et al. (US 5,891,641) or Martinez et al. (WO 98/41872) and 2) Tsien et al. (US 5,998,204) in view of 3) Eberwine et al. (WO 96/05847) and 4) Epps et al. (US 6,203,994) or Kinjo et al. (Nucleic Acids Research, 1995) is hereby, withdrawn.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-2, 4-8, and 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step a) is vague and indefinite in reciting, "which can generate a signal in a manner dependent on the binding of the first binding partner to the protein" because in reciting, "can", it fails to recite a positive limitation in the claim.

Claim 2, step b) is vague and indefinite in reciting, "which can generate a signal in a manner dependent on said post-translational modification" because in reciting, "can", it fails to recite a positive limitation in the claim.

Claim 13 is indefinite because it appears grammatically redundant in reciting, "removing unbound labeled first binding partner is removed to allow ...".

**New Matter**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 4-8, 10-14, and 19-22 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reason of record and reiterated as follows.

In this case, the specification does not appear to provide any literal or descriptive support for the recitation of "a labeled second binding partner which binds to said protein in a manner dependent on the conformational state of said protein and which can generate a signal in a manner dependent on the binding of the first binding partner to the protein" and "a second labeled binding partner ... which can generate a signal in a manner dependent on said post-translational modification". The specification at page

7, line 13 bridging to page 8, line 1 and pages 19-21 describes both the first and second binding partners as being labeled and detected by FRET, wherein two fluorescent labels fluoresce in close proximity with each other. According to Applicant, similar configurations include use of enzyme domains. Applicant's disclosure further provides that the second binding partner does not bind in a strictly conformation-dependent manner but is capable of binding to a subset of possible conformations or substantially all conformations, of the protein. Nowhere, however, in the specification provides literal or descriptive support for the recitation of "a labeled second binding partner which binds to said protein in a manner dependent on the conformational state of said protein and which can generate a signal in a manner dependent on the binding of the first binding partner to the protein" and "a second labeled binding partner ... which can generate a signal in a manner dependent on said post-translational modification". Furthermore, none of the originally filed claims recited the limitation in question. Recitation of claim limitation lacking literal support in the specification or originally filed claims constitutes new matter.

***Double Patenting***

10. Claims 1, 4-8, 10-14 and 19-22 stand provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-13 and 18-21 of copending Application No. 09/258,452. This is provisional double patenting rejection is being maintained for reason of record.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prusiner et al. (US 5,891,641) in view of Foster et al. (US 4,444,879) for reason of record or reiterated as follows.

Prusiner et al. disclose a method for determining a diseased related conformational state of a protein such as PrP<sup>Sc</sup> in a sample (see column 5, lines 21-58). Prusiner et al. specifically disclose contacting the protein with a labeled antibody that binds (has a higher binding affinity) to the protein in a manner dependent on the conformational state of the protein; i.e. PrP<sup>C</sup> (native or non-disease state) or PrP<sup>Sc</sup> (diseased conformation) (see column 4, lines 24-56, column 12, lines 4-28, and column

Art Unit: 1641

17, lines 49-58). The antibody is detectably labeled with fluorophores, radioisotopes, enzymes, etc. so as to detect labeling of the protein wherein a generation of signal is indicative of the conformational state of the protein (see column 12, lines 64-67).

Prusiner et al. also disclose contacting the protein with a second antibody or capture ligand to immobilize the protein on a solid phase substrate (see column 4, lines 5-10).

Prusiner et al. also disclose that recombinant prion proteins can be covalently linked (chemically crosslinked) to a solid phase substrate (polystyrene plates) (see column 6, lines 1-3). Standard preparations of disease related conformational state proteins such as prion proteins are produced for use in calibration and validation testing of the diagnostic sensitivity, specificity and predictive values of the assay (see column 22, lines 58-61). Antibody binding to the disease related conformation is measured using time resolved, dissociation enhanced fluorescence (see column 17, lines 62-65).

Prusiner et al. have been discussed supra. Prusiner et al. differ from the instant invention in failing to incorporate the protein standards, binding partners, labels, and packaging components into a kit format.

Foster et al. disclose controls, reagents including antibodies and labels, and instructions in a kit format for use in assay methods.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have incorporated the protein standards, binding partners and label reagents taught by Prusiner into a kit format as taught by Foster et al., for use in a method of determining the conformational state of a protein because kit formats are recognized for their advantage in convenience and economy.

**Prior Art**

12. Claims 1, 4-8, and 10-14, as amended, are clear of the prior art of record.
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

grg  
December 15, 2002 S:

*Christopher L. Chin*  
CHRISTOPHER L. CHIN  
PRIMARY EXAMINER  
GROUP 1641

12/15/02